Claims

We claim:

1. A composition that comprises liposomes stably associated with at least one water-soluble camptothecin and at least one fluoropyrimidine at a camptothecin-to-fluoropyrimidine mole ratio that has a desired cytotoxic, cytostatic or biologic effect to relevant cells or tumor cell homogenates.

2. The composition of claim 1 wherein the desired cytotoxic, cytostatic or biologic effect to relevant cells or tumor cell homogenates is non-antagonistic.

3. The composition of claim 1 which further includes leucovorin sufficient to stabilize said fluoropyrimidine.

4. The composition of claim 2 which further includes leucovorin sufficient to stabilize said fluoropyrimidine.

5. The composition of claim 1 wherein the water-soluble camptothecin is irinotecan (CPT-11), topotecan, 9-aminocamptothecin or lurtotecan.

6. The composition of claim 1 wherein the water-soluble camptothecin is a hydrophilic salt of a water-insoluble camptothecin.

7. The composition of claim 2 wherein the water-soluble camptothecin is irinotecan (CPT-11) or topotecan.

8. The composition of claim 1 wherein the fluoropyrimidine is floxuridine, fluorouracil or UFT (tegafur/uracil).

9. The composition of claim 1 wherein said liposomes comprise a phosphatidylcholine-containing lipid.

10. The composition of claim 9 wherein said phosphatidylcholine-containing lipid is DSPC or DAPC.

11. The composition of claim 1 wherein said liposomes comprise a phosphatidylglycerol or a phosphatidylinositol.

12. The composition of claim 11 wherein the phosphatidyl glycerol is DSPG or DMPG.

13. The composition of claim 1 wherein said liposomes comprise a sterol.

14. The composition of claim 13 wherein said sterol is cholesterol.

15. The composition of claim 14 wherein said cholesterol is present at less than 20 mol%.

16. The composition of claim 1 wherein said liposomes comprise a metal ion solution.

17. The composition of claim 16 wherein said metal ion is copper.

18. The composition of claim 17 wherein said metal ion solution is $Cu(gluconate)_2$ or $CuSO_4$.

19. The composition of claim 1 wherein said water-soluble camptothecin and fluoropyrimidine are co-encapsulated.

20. The composition of claim 1 wherein said water-soluble camptothecin is irinotecan or topotecan and said fluoropyrimidine is floxuridine or 5-FU.

21. The composition of claim 20 wherein said liposomes comprise DSPC.

22. The composition of claim 20 wherein said liposomes comprise DSPG.

23. The composition of claim 20 wherein said liposomes comprise cholesterol.

24. The composition of claim 20 wherein said liposomes comprise $Cu(gluconate)_2$ or $CuSO_4$.

25. The composition of claim 20 wherein said liposomes comprise triethanolamine (TEA).

26. The composition of claim 1 which, when administered to a subject, provides a therapeutic activity greater than that which is obtained when said water-soluble camptothecin and said fluoropyrimidine are administered in the same ratio but not stably associated with liposomes.

27. The composition of claim 1 wherein the composition comprises a third agent.

28. A method to prepare a composition comprising liposomes, said liposomes having stably associated therewith at least one water-soluble camptothecin and one fluoropyrimidine in a mole ratio which is non-antagonistic, which method comprises

a) determining in a relevant cell culture assay, cell-free assay or tumor cell homogenate for biological activity a mole ratio of said water-soluble camptothecin and fluoropyrimidine agents which is non-antagonistic over at least 5% of the concentration range over which greater than 1% of cells are affected ($f_a > 0.01$) by said ratio of agents, and

b) encapsulating within said liposomes a mole ratio of water-soluble camptothecin-to-fluoropyrimidine determined to be non-antagonistic in step a).

29. A method to treat a disease condition in a subject which method comprises administering to a subject in need of such treatment a therapeutically effective amount of the composition of claim 1.

30. The method of claim 29 which further comprises administering leucovorin to said subject.

31. The method of claim 29 wherein the subject is a human.

32. The method of claim 29 wherein the subject is a non-human mammal or avian.

33. A method to deliver a therapeutically effective amount of a fluoropyrimidine/water-soluble camptothecin drug combination by administering a fluoropyrimidine stably associated with a first delivery vehicle and a water-soluble camptothecin stably associated with a second delivery vehicle wherein the ratio of the fluoropyrimidine and the water-soluble camptothecin administered is non-antagonistic.